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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENT
(Chapter II of the Patent Cooperation Treaty)

REC'D 16 JUL 2004
PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 100696-1 Wo	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/SE 2003/000614	International filing date (day/month/year) 15.04.2003	Priority date (day/month/year) 18.04.2002
International Patent Classification (IPC) or national classification and IPC C07D 491/22, A61K 31/438, A61K 31/439, A61P 25/00		EPO - DG 1 20.09.2004
Applicant AstraZeneca AB et al		(37)

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 7 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
 - ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 31.10.2003	Date of completion of this report 07.07.2004
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Eva Johansson/BS Telephone No. +46 8 782 25 00

Form PCT/IPEA/409 (cover sheet) (January 2004)

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/Se 2003/000614

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished

pages* _____ as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to the sequence listing *(specify)*: _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/Se 2003/000614

Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

The priority is considered valid.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/Se 2003/000614

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 14-17

because:

☒ the said international application, or the said claims Nos. 14-17 relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. "

PCT/Se 2003/000614

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>1-13, 18-22</u>	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	<u>1-13, 18-22</u>	NO
Industrial applicability (IA)	Claims	<u>1-13, 18-22</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents were cited in the search report:

D1) WO 9903859 A1
D2) WO 0042044 A1
D3) WO 0045846 A1

The claimed invention relates to novel spiro[1-azabicyclo[2.2.2]octane-3,2' (3'H)-furo[2,3-b]pyridine] derivatives, which are potent ligands for nicotinic acetylcholine receptors (nAChR's) and can be used for the treatment of disorders related to this ligand.

D1, which is considered to be the most relevant document, relates to structurally very close compounds with the same therapeutical use. The claimed compounds only differ from the known compounds through the substitution on the furo[2,3-b]pyridine group in the 5' position. In the claimed compounds the substitution represents an eventually substituted "thiophenyl" or "benzothiophenyl", group while the substitution in known compounds represents listed from examples 15-18, 21-22 and 38 of "morpholino", "azetidiny", "pyridyl", "furyl" or "piperazinyl" group.

The differences consist consequently of structurally close heterocyclic groups.

The problem to be solved by the present invention may therefore be regarded as novel spiro[1-azabicyclo[2.2.2]octane-3,2' (3'H)-furo[2,3-b]pyridine] derivatives which are potent ligands for nicotinic acetylcholine receptors (nAChR's) and can be used for the treatment of disorders related to this ligand.

.../...

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/Se 2003/000614

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: BOX V

This is achieved with the novel derivatives.

Regarding the cited document above, it would be obvious to a person skilled in the art to prepare the claimed compounds and that the novel compounds would achieve the same therapeutical effect as the known compounds in D1.

The paragraphs on pages 11-12 regarding the pharmacology tests describe tests that are the same tests as in D1. The applicant has not shown that the claimed compounds are likely to have any unexpected beneficial effect over the prior art.

Thus, the claimed invention in claims 1-13 lacks inventive step.

Claims 18-20, which relate to the compounds wherein one or more of the atoms is a radioisotope and to the use the compounds in screening, are considered to involve particular executions obvious to a person skilled in the art for which patent protection is not justified. Thus, claims 18-20 lack inventive step.

Claims 21 and 22 relate to spiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine] derivatives as intermediate for the preparation of the claimed compounds.

D2 relates to structurally close spiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine] derivatives as intermediate (structure VI) for the preparation of 5' or 6' substituted spiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine] derivatives.

Thus, claims 21-22 lack inventive step.

D3 relates to pharmaceutical compositions containing nicotine or a ligand of nicotine receptors and a monamine oxydase inhibitor and their use.

D3 discloses the general state of art and is not considered to be of particular relevance.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/Se 2003/000614

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
US 2003/0018042	23.01.2003	31.05.2002	
WO 02/096912	05.12.2003	29.05.2002	01.06.2001

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)

Date of written disclosure
referring to non-written disclosure
(day/month/year)

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